REMARKS

Claims 1-37 are pending in the application. Claims 1-17 are withdrawn from consideration. Claims 18-37 are presented for further consideration. Applicants respectfully request reconsideration of the pending claims in light of the comments presented below.

Rejections under 35 U.S.C. § 102(b)

Claims 18, 25, and 27

Claims 18, 25, and 27 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 4,240,751 to Linnecke and Wong (hereinafter "Linnecke").

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference ... There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). As discussed below, the claims of the present application are not anticipated by the cited reference, because Linnecke does not teach each and every element of the rejected claims.

According to the Examiner, Linnecke discloses every limitation of the rejected claims by teaching a latex agglutination assay in which ligands for a desired analyte are non-covalently bound to a latex bead and upon binding to the analyte, the latex beads condense and are detected spectrometrically. *Office Action* of April 7, 2010, page 3. Applicants respectfully disagree.

Claim 18 recites an assay system comprising a suspension of colloidal particles, wherein said colloidal particles are near a dynamical phase transition state. The transition state can be wherein the beads are condensed together, near a transition to a dispersed state, or wherein the beads are dispersed, and near a transition to a condensed state. This differs from the agglutination assay recited by Linnecke. Examples IV, V and VI of Linnecke both refer to experiments wherein latex beads were coated with an antigen. Those beads were then contacted by an antibody. In Example IV, the antibody is anti-HCG, in Example V the antibody is a gonococcal antibody, and in Example VI the antibody is rheumatoid factor. In each experiment the colloidal

particles are not near a dynamical phase change prior to addition of the antibody which results in agglutination of the sample.

As discussed in the specification, a dynamical phase transition state is a state wherein relatively minor perturbation of the latex beads leads to a dynamical transition from one state into another. In this phase change virtually the entire population moves from one phase to another. At the particle level, each particular particle pairs and un-pairs an arbitrary number of times, and never irreversibly associates with one another. (Spec. at [0033]). This differs from the recited agglutination assay in Linnecke, wherein detection relies upon an antibody to agglutinate a portion of the antigen-covered particles in a clump that is detected. In Linnecke, the addition of antibody merely clumps together beads without regard to whether or not the beads were near the claimed dynamical phase transition state. Similarly, Linnecke nowhere teaches an assay wherein condensed beads-antibodies are near the non-agglutinated state prior to adding test sample or that relatively minor perturbation of the agglutinated beads can lead to dynamic loss of agglutination. Indeed, such an assay is unlikely to work under the antibody-antigen conditions described by Linnecke.

Because Linnecke fails to disclose a suspension of colloidal particles near a dynamical phase transition state, Linnecke does not anticipate Claims 18, 25, and 27 under 35 U.S.C. § 102(b). For this reason, Applicants respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 103(a)

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (CCPA 1974). Obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. *In re Rinehart,* 531 F.2d 1048, 1051 (CCPA, 1976). The PTO bears the burden of establishing a case of *prima facie* obviousness. See *In re Fine*, 837 F.2d 1071, 1074 (Fed Cir. 1988). Applicants respectfully assert that a *prima facie* obviousness has not been shown because the cited references, in combination with the knowledge of one of skill in the art, do not teach or suggest all of the claim limitations.

As discussed above, Applicants' independent claims are directed to "a suspension of colloidal particles... wherein said colloidal particles are near a dynamical phase transition state..." and "a suspension of colloidal particles, wherein said particles are coated with a lipid layer." Claims 18 and 28. Linnecke, in combination with the knowledge of one of ordinary skill in the art and each of the secondary references discussed below, fails to teach or suggest all of the claim limitations in the independent (and therefore dependent) claims. Further, as discussed below, it would not have been obvious to modify the Linnecke agglutination assay to arrive at the assays of the present application.

Claims 19-21 and 30

Dependent Claims 19-21 and 30 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke in view of Singh *et al.* (U.S. Patent Publication No. 20020034827). Singh *et al.* discloses general methods and materials for the extraction and analysis of complex materials. *See* Singh *et al.*, Abstract.

Claim 19 recites "a first population and a second population of colloidal particles," while Claim 20 recites larger colloidal particles in the first population. Claim 21 recites different labeling in the first and second population, while Claim 30 recites a means for detecting comprising a fluorescence detector.

Although Linnecke does not disclose more than one population of colloidal particles, the Examiner asserts that it would have been obvious for a skilled artisan to use at least two populations of nanoparticles in the agglutination assay of Linnecke with a reasonable expectation of success. *Office Action*, at pp. 3-4. However, the Singh *et al.* reference discloses only general concepts regarding the extraction and analysis of complex materials and does not supply the claimed limitations that Linnecke fails to disclose as discussed above.

Furthermore, there is no apparent reason to use at least two populations of latex beads in the Linnecke agglutination assay with any reasonable expectation of success. According to the Examiner, a skilled artisan would be motivated to use at least two populations of nanoparticles to analyze complex biological compositions comprising two or more analytes of interest according to Singh. *Office Action*, page 4.

The agglutination assay Linnecke, however, is a simple diagnostic test to detect whether a patient's specimen is positive or negative for the presence of a single analyte. For instance, Linnecke in Examples IV-VI teaches use of the latex bead agglutination assay to detect presence of pregnancy hormone in urine, gonococcal antibody in serum, or rheumatoid factor in serum. A person of ordinary skill in the art would have no reason to modify the Linnecke test to include at least two populations, especially since such a modification offers no apparent advantage to detecting the pregnancy hormone, gonococcal antibody, or rheumatoid factor and could interfere with their detection. A person of ordinary skill would be discouraged from modifying the Linnecke agglutination assay to include at least two populations because doing so could cause disruption of each population's binding to the single analyte being detected. Furthermore, a person of ordinary skill would not introduce two or more populations to the Linnecke assay because it is unclear how to distinguish which population(s) bound to the analyte or underwent a phase transition by measuring light transmission of the reaction sample. These problems with introducing more populations to the Linnecke agglutination test indicate that a person of ordinary skill would not combine the teachings of Linnecke and Singh, and that their combination could not be accomplished with a reasonable expectation of success.

Based on the foregoing, Linnecke fails to teach or suggest all of the claim limitations of Claims 19-21 and 30 in view of Singh *et al.* Further, one of skill in the art would not have been motivated to combine the Linnecke and Singh *et al.* references to arrive at the assays of Claim 19-21 and 30, nor would one of skill in the art have arrived at the assays with a reasonable expectation of success.

Claims 22-24, 28, and 32

Dependent Claims 22-24, 28, and 31 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke in view of Schaertl *et al.* (*J Biomol Screen* 2000; 5(4):227-237). Schaertl *et al.* discloses the labeling of nanoparticles for immunoassays. *See* Schaertl *et al.*, Abstract.

Claims 22 and 28 recite a lipid layer, while Claims 23 and 31 recite a natural cell membrane. Claim 24 recites covalent linking between the ligand and colloidal particle.

Although Linnecke does not disclose a lipid layer, the Examiner asserts that the nanoparticle of Schaertl *et al.* inherently includes a lipid layer and could be used to increase the range of analytes for detection in Linnecke. *Office Action*, page 5. However, the Schaertl *et al.* does not provide the claimed limitations that Linnecke fails to disclose as discussed above.

Additionally, Schaertl discloses live bacteria as the source of lipid bilayer. A person of ordinary skill would not have known how to adapt the natural lipid bilayer of a live bacterium onto the latex beads of Linnecke with any reasonable expectation of success. Nor would there have been any motivation to make such a modification. In the claimed system, the lipid layer is used to maintain the colloidal particles near the claimed phase transition state. However, a person of ordinary skill would not combine the live bacteria of Schaertl with the latex beads of Linnecke because it would be unclear whether a hypothetical bacterium-latex bead structure could even be used in a agglutination assay. One of ordinary skill in the art would likely believe that such a lipid layer would interfere with binding of the bead-bound antigen to the antibody being analyzed, as opposed to being any kind of improvement in such an assay. Indeed, the bacteria in Schaertl are used in a fluorescence based detection assay, suggesting that a person of ordinary skill would not be able to use the bacteria with any reasonable expectation of success in the Linnecke agglutination assay, which is analyzed spectroscopically by light transmission.

As such, Linnecke fails to teach or suggest all of the claim limitations of Claims 22-24, 28, and 31 in view of Schaertl *et al.* Moreover, there is also no motivation to make the claimed combination because one of ordinary skill in the art would not believe that such a combination would have a reasonable chance of success to operate for its intended purpose.

Claim 26

Dependent Claim 26 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke.

Claim 18 recites an assay for detecting the binding of an analyte to a ligand by determining transition from a first to a second phase, while Claim 26 recites that the first phase is a condensed phase and second phase is a dispersed phase.

Linnecke fails to establish a *prima facie* case of obviousness because it fails to disclose each and every limitation of the claim. As discussed above, Linnecke fails to disclose a

suspension of colloidal particles near a dynamical phase transition state wherein each colloidal particle comprises a single central particle associated with more than one copy of a ligand.

Claim 29

Dependent Claim 29 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke in view of Faulds *et al.* (*Analyst* 2002; 127:282-86). Faulds *et al.* discloses the use of a microscope to detect light scattering of gold or silver colloid surfaces. Faulds *et al.*, Abstract.

Claim 29 recites detection using a microscope.

As discussed above, Linnecke, in combination with the knowledge of one of skill in the art, does not teach or suggest all of the claim limitations of Claim 28 or the claims depending therefrom (including Claim 29). As such, the combination of Linnecke and Faulds fails to establish a prima facie case of obviousness with respect to Claim 29.

Claims 33-35, and 37

Dependent Claims 33-35 and 37 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Linnecke in view of Strauss (US 4410660). Strauss discloses silica or metal particles.

As discussed above, Linnecke does not teach or suggest a single central particle associated with more than one copy of a ligand specific for an analyte. As such, the combination of Linnecke and Strauss fails to establish a prima facie case of obviousness with respect to Claims 33-35 and 37, which depend from Claim 18 or 28 and characterize the single central particle.

Based on the foregoing, Linnecke, in combination with the knowledge of one of skill in the art and the cited references, does ***not*** teach or suggest all of the claim limitations, nor would it have been obvious to modify the assay of Linnecke to arrive at the claimed methods. Applicants therefore respectfully request withdrawal of the rejections under 35 U.S.C. § 103(a).

CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. In light of the above amendments and remarks concerning the pending claims, Applicants respectfully request allowance of the pending claims. If the Examiner has any questions which may be answered by telephone, the Examiner is invited to call the undersigned directly.

No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: July 8, 2010

By: _____

Michael L. Fuller
Registration No. 36,516
Attorney of Record
Customer No. 20995
(619) 235-8550

9238401/SRL
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